

A Clinical Study of 'Sus-Phrine,' an Aqueous Epinephrine Suspension for Sustained Action

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FOR the past fifty years epinephrine has been the essential drug used in reversing the functional disturbances occurring in allergic diseases, namely, spasm of smooth muscles, capillary dilation and permeability, and hypersecretion of various glands. These reactions if not reversed often lead to unfavorable sequelae such as chronic bronchial asthma, urticaria, angioneurotic edema, local and generalized pruritus, with associated or concomitant anxiety.

Epinephrine is the chief drug of the sympathomimetic group and is so called because it exerts its beneficial effects by mimicking or simulating the action produced by the stimulation of sympathetic nerves. Its action, however, is of short duration and must be given at frequent intervals by injection or as an aerosol, particularly for allergic bronchitis and bronchial asthma, thereby producing discomfort to the patient and shortening the periods of rest which the anxious, irritable and frequently exhausted allergic patient needs.

The objection to the short duration of action of epinephrine was met to some extent many years ago by placing the drug in peanut oil or in gelatin. The viscosity of these vehicles, however, made it necessary to shake vigorously and often warm the material to render it in a form suitable for injection deep in the gluteal muscles with a large, long needle. Often, the intensity and duration of action of the drug were unpredictable. During the cold weather when the ampoules or vials were carried in the physician's bag it was even more difficult to aspirate the material into the syringe. Frequently some of the oil leaked on the bed-clothes of bedridden patients and the undergarments of ambulatory patients. This aspiration of material and preparation of the patient required valuable time and on occasions the needle would become plugged necessitating a second, and often a fear provoking, injection.

Epinephrine in oil, however, has been of great value as a medicinal agent of prolonged action in the symptomatic treatment of allergic diseases. It certainly has reduced the number of injections usually required with the aqueous solution. However, because of the inconveniences exhibited and its demand for the patient's and physician's time we became interested in the recently available aqueous suspension of epinephrine known as Sus-Phrine.* It contains epinephrine 1-200, phenol 0.5 per cent, sodium thioglycollate 0.5 per cent in a sterile buffered solution containing 25 per cent glycerine in distilled water.

This free flowing aqueous suspension represents a distinct departure from the previously available heavy, viscous preparations and it possesses marked advantages chiefly because of the small quantity of the drug required for therapeutic action and ease of administration. The material is injected subcutaneously which necessitates only a small 1/2 inch, 26 gauge needle. Selected patients may be taught to give themselves injections similar to insulin injections by diabetics. There is relatively minimal irritation after injection. Occasionally there is a stinging effect which persists for one to three minutes. There is less likelihood of abscess formation, less expense to the patient and a saving of the physician's time.

Since the material permits the use of a short, small needle, it diminishes the psychological fear reaction which the sight of a long, large needle elicits in youngsters and in nervous apprehensive adults.

Naterman recently found this aqueous suspension is particularly useful in patients who ordinarily require frequent injections of an aqueous solution of epinephrine 1:1000 to control asthmatic attacks,¹ urticaria and angio-neurotic edema.

Our clinical study dealt with the use of Sus-Phrine in seventy-eight patients in the clinic, office and home. The group consisted of fifty-two bronchial asthmatics of the perennial type, eighteen

* "Sus-Phrine" for this study was generously supplied through the courtesy of Brewer & Company, Worcester, Mass.

cases of pollinosis (hay fever) with associated seasonal pollen asthma, two cases of angioneurotic edema and six patients with urticaria resulting from drug allergy. The ages ranged from three to sixty-nine years. The dosage levels varied from 0.1 c.c. to 0.4 c.c. depending upon the patient's age: 1-5 yrs. 0.1 c.c., 5-10 yrs. 0.2 c.c., 10-15 yrs. 0.3 c.c., and over 15 yrs. 0.4 c.c. However, assuming the average weight of an adult to be 150 lbs. a child weighing 75 lbs., could receive one-half the adult dose or 0.2 c.c. All injections were given subcutaneously in the lateral surface of the upper arm with a 1/2 inch 26 gauge needle.

The material does not require refrigeration and its therapeutic efficiency is not diminished should the suspension become discolored as shown by others.² The suspension is easily injected in readily accessible areas of the upper arms.

Recently we have used Sus-Phrine in five cases of status asthmaticus in conjunction with corticotropin and observed that the dosage of the adrenocorticotrophic hormone could be more rapidly reduced and the intervals between doses prolonged.

Because of the complexity of the allergic process the injections were given in conjunction with aqueous epinephrine solution, aminophyllin, antihistamines and sedatives when indicated. Bronchiolar spasm, edema, nasal congestion and pruritis were greatly relieved in bronchial asthma, hay fever and urticaria respectively.

In patients receiving hyposensitization therapy for bronchial asthma and hay fever, with bronchiolar spasm, nasal blockage and eye symptoms present, the drug was given in the same syringe with the allergen.

At the beginning of the study Sus-Phrine (given subcutaneously) was used alternately with adrenalin in oil (given deep in the gluteal muscle) for five injections each on ten patients, to determine by comparison its therapeutic effectiveness. Initial therapeutic benefit or symptomatic relief was observed by the patients within 10-22 min. (average 16 min.), with the duration of action 5-10 hrs. (average 7½ hrs.) for Sus-Phrine, as compared to an initial action of 24-32 minutes (average 28 min.) and 4-9 hrs. duration (average 6½ hrs.) for adrenalin in oil.

The side reactions were tachycardia, palpitation, lightheadedness and jitteriness in five patients,

transient anesthesia of the fingers in one and insomnia in one. These untoward effects may be attributed to epinephrine as they were similar, but slightly more pronounced in the same individuals, with the additional side effect of nausea in one patient, with adrenalin in oil. Because of the increased pharmacologic sensitivity or decreased tolerance to epinephrine in some patients, we found it advisable to give an initial dose of 0.05 c.c. to children and 0.1 c.c. to adults in order to determine tolerance to the drug. The determined dosage, according to age level and tolerance, may be repeated at six to eight hour intervals.

The infrequency of injections without the necessity of placing patients in a prone position to expose the gluteal muscles for deep injections saves time and reduces the nursing load. This is of considerable value in handling bed confined patients in the home.

SUMMARY AND CONCLUSIONS

1. The action of epinephrine may be prolonged in treating allergic diseases by the use of a stable suspension of epinephrine in glycerine and distilled water. The product used for our study is marketed as 'Sus-Phrine.'

2. Our clinical study dealt with a group of seventy-eight patients, which consisted of fifty-two perennial bronchial asthmatics, eighteen cases of pollinosis (hay-fever) with associated seasonal bronchial asthma, two cases of angioneurotic edema and six cases of urticaria resulting from drug allergy.

3. The free flowing suspension with the small dosages required (0.1 c.c. to 0.4 c.c.) permits the use of a tuberculin syringe and a 26 gauge needle with minimal discomfort to the patient. This is a distinct advantage in treating children and apprehensive adults.

4. The initial therapeutic effect was observed by the patient within 10-22 minutes (av. 16 min.) with a duration of action of 5-10 hours (av. 7½ hrs). 'Epinephrine fastness' was not observed in our study.

5. The potency of the suspension is maintained over long periods of time and its therapeutic efficiency is not decreased by discoloration of the material.

6. Sus-Phrine is a valuable therapeutic adjunct in the treatment of bronchial asthma, urticaria and

angioneurotic edema, because of the prolonged epinephrine action, mode of administration and small dosages required, with fewer and less pronounced side reactions than any of the other long acting epinephrine compounds now available.

LITERATURE CITED

1. NATERMAN, H. L. Ephinephrine Base Suspended in Water with Thioglycolate. *J. Allergy* 24:60, 1953.
2. UNGER, A. H. and L. UNGER. Prolonged Epinephrine Action. *Ann. Allergy*, 10:128-130, 1952.

EGYPTIAN GYNECOLOGY

Knowledge of a woman whose sight is painful, whose neck aches. Say thou as to it: It is the fall of the womb in her eyes. Do thou for her (thus): *kap* (anoint ?) her with incense and fresh oil: *kap* her vulva with it *kap* her eyes with the shank of a swallow (?); do thou let her eat the liver (?) of an ass raw.

Knowledge of a woman whose uterus is painful is carrying (?). Say thou as to it: what dost thou smell? If she says to thee I smell roast meat, say thou as to it, it is the nemsu of the uterus, do thou for her (thus): *kap* her with everything that she smells like roast meat.

Knowledge of a woman whose posterior, belly, and branching (?) of her thighs are painful. Say thou as to it: it is the falling of the womb. Do thou for her (thus): *uab* grains, 1/64 *bekt*; *shasha* fruit 1/64 *bekt* cow's milk 1 *henu*. Cook, let it cool, make it into one mess (gruel), drink four mornings.

Knowledge of a woman (pained) in her belly and vulva the surroundings (?) *dadat* if her vulva between her thighs. Say thou as to it, it is the growing very big of birth. Do thou for her (thus), fresh oil one *henu*, pour upon (?) her vulva.

Knowledge of a woman pained in her teeth and jaws; she knows not (how to open ?) her mouth. Say thou to her it is the itching (?) (determinative a *tooth*) of the vulva. Do thou for her (thus): *kap* her with oil and incense in a bowl (?) pour on her . . . the urine of an ass that has engendered two colts on the day that it is passed it (the urine). If her . . . is pained from her . . . shoulder (?) to her hips . . .

Knowledge of a woman ill in all her limbs and the sockets of her eyes. Say thou as to it: it is constriction (?) of the uterus; she cannot *drink beer at all* (?), or: is altogether starved as one who has recently given birth. Do thou for her (thus) . . . of *ab* in water, drink (4 ?) mornings.

Knowledge of a woman pained in her feet (?) and legs after walking. Say thou as to it: it is falling of the womb. Do thou for her (thus). Rub her feet and legs with handrubbing until she is well.

Knowledge of a woman pained in her neck, belly and ears, she does not hear speech. Say thou as to it: it is violence (?) of the uterus. Do thou for her (thus): like that medicine for destroying putrefaction (?) of the womb.

Knowledge of a woman pained in her vulva and all her limbs like one beaten. Say thou with regard to it: it is . . . of the womb. Do thou for her (thus): (Let her) eat oil (fat?) until she is well.

Knowledge of a woman whose urine pains her like the . . . of . . . urine. Say thou with regard to it: it is falling of the womb. Do thou for her (thus) *aurit*, corn, *sherni*, *met ent gen*: pound, grind fine, upon *ndadat*—beer one *henu*: cook and drink four mornings. Let her wait lying down fasting; next morning let her drink one *henu* of the same: let her wait fasting until the time of . . . washing the mouth (?).

Knowledge of a woman who loves the bed, she does not rise and does not . . . it (?). Say thou with regard to it: it is the grasping (?) of the womb. Do thou for her (thus): let her drink 2 *henu* or *kbani*, let her vomit it immediately.

Knowledge of a woman pained in her legs. Give thou to her strips of fine linen soaked in anti (frankincense ?) . . . (if her movements are) pleasant (?) in her doing everything it is health, if (her movements are painful ?) say thou to her) it is (. . . of the womb). Do thou for her (thus): a *mehui* vase of fresh oil, soak . . . put anti (frankincense ?) on her . . . after doing this.

Knowledge (of a woman pained in her . . .) in her legs, in one side . . . Say thou with regard to it: it is bending (?) (of the womb). Do thou for her (thus) . . . corn, *sheni*, *saam met-ent-gin* (pound, grind fine, etc. . . .) the side in which she is pained: let her lie upon it. If returns . . . let her eat it, two . . . of . . . mixed with . . . if she passes (urine ?) sitting (?) in doing everything (she will be well? if) . . . swollen, put thy finger upon it, if thou find it tough . . . if . . . upon the uterus, it is colic?

Knowledge of a woman thirsty . . . (say thou with regard to it) . . . do thou for her (thus): glue *shebeb* 1/64 *bekt*, glue suit . . . altogether.

Knowledge of a woman whose belly is swollen . . . (say thou with regard to it) . . . (do thou) for her (thus): *malachite* 1/64 *bekt*, pound, grind fine, cook in cow's milk in a . . . (drink it) four. . . .

Knowledge of a woman pained in all her limbs and the sockets of (her) eyes . . . *kemt*. Say thou with regard to it it is *kemt* of the womb. Do thou for her thus: oil . . . *aart*, *nekant*, *aub*, corn, *sheni* . . . pound, grind fine, cook, drink four days. *The Kabun Papyrus*, ca. 2000 B.C., *Griffith's Translation*.